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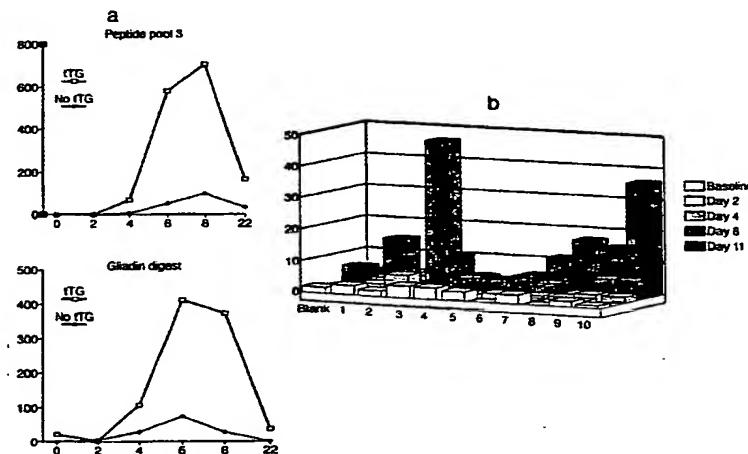
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(54) Title: DIAGNOSIS OF COELIAC DISEASE USING A GLIADIN EPITOPE



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(57) Abstract: A method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual comprising : (a) contacting a sample from the host with an agent selected from (i) the epitope comprising sequence which is : SEQ ID NO : 1 or 2, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO : 3, (ii) an epitope comprising sequence comprising : SEQ ID NO : 1, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO : 3, which epitope is an isolated oligopeptide derived from a gliadin protein, (iii) an analogue of (i) or (ii) which is capable of being recognised by a T cell receptor that recognises (i) or (ii), which in the case of a peptide analogue is not more than 50 amino acids in length, or (iv) a product comprising two or more agents as defined in (i), (ii) or (iii), and (b) determining *in vitro* whether T cells in the sample recognise the agent; recognition by the T cells indicating that the individual has, or is susceptible to, coeliac disease. Therapeutic compositions which comprise the epitope and gliadin proteins which do not cause coeliac disease are also provided.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03760

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G01N33/68 C07K14/415 A61P37/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, CHEM ABS Data, BIOSIS, EMBASE, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|---------------------------|
| X | O'KEEFFE J ET AL: "T cell proliferation, MHC class II restriction and cytokine products of gliadin-stimulated peripheral blood mononuclear cells (PBMC)." CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104 the whole document | 1-3, 6-12, 22-26,37 |
| X | EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN (NL)) 31 March 1999 (1999-03-31) the whole document | 12, 14-22, 25-59 |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|---------------------------|
| X | VAN DE WAL YVONNE ET AL: "Small intestinal T cells of celiac disease patients recognize a natural pepsin fragment of gliadin." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 17, 18 August 1998 (1998-08-18), pages 10050-10054, XP000982626 Aug. 18, 1998 ISSN: 0027-8424 the whole document --- | 1-3, 6-12, 22-26,37 |
| X | TRONCONE R ET AL: "Cytokines produced by gliadin-specific T cell clones from the coeliac mucosa." GASTROENTEROLOGY, vol. 110, no. 4 SUPPL., April 1996 (1996-04), page A1031 XP000989625 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week; San Francisco, California, USA; May 19-22, 1996 ISSN: 0016-5085 abstract --- | 1-3, 6-12, 22-26,37 |
| X | GODKIN A J ET AL: "Identification of a coeliac disease-specific T cell epitope from A-gliadin." GUT, vol. 44, no. SUPPL. 1, April 1999 (1999-04), page A72 XP000989626 British Society of Gastroenterology Annual Meeting; Glasgow, Scotland, UK; March 23-25, 1999 ISSN: 0017-5749 abstract --- | 1-3, 6-12, 22-26,37 |
| A | OKITA T W ET AL: "EVOLUTION AND HETEROGENEITY OF THE ALPHA-BETA-TYPE AND GAMMA-TYPE GLIADIN DNA SEQUENCES" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 260, no. 13, 1985, pages 8203-8213, XP000982597 ISSN: 0021-9258 the whole document -& DATABASE SWISSPROT 'Online' ID: GDA4_Wheat ACC: P04724, 13 August 1987 (1987-08-13) XP002161985 abstract --- | 38-59 |
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International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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|----------|---|-----------------------|
| X | <p>UHLIG H ET AL: "Role of tissue transglutaminase in gliadin binding to reticular extracellular matrix and relation to coeliac disease autoantibodies." AUTOIMMUNITY, (1998) 28 (4) 185-95. , XP002118954 page 186, left-hand column, paragraph 2 -----</p> | 13 |
| P, X | <p>ANDERSON ROBERT P ET AL: "In vivo antigen challenge in celiac disease identifies a single transglutaminase-modified peptide as the dominant A-gliadin T-cell epitope." NATURE MEDICINE, vol. 6, no. 3, March 2000 (2000-03), pages 337-342, XP000982628 ISSN: 1078-8956 the whole document -----</p> | 1-34, 37 |
| P, X | <p>ARENTH-HANSEN, HELENE ET AL: "The intestinal T cell response to alpha-gliadin in adult celiac disease is focused on a single deamidated glutamine targeted by tissue transglutaminase" J. EXP. MED., vol. 191, no. 4, 21 February 2000 (2000-02-21), pages 603-612, XP000986723 the whole document -----</p> | 1-34, 37 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim(s) 5 and 40 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

And although claims 41 and 42 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

INTERNATIONAL SEARCH REPORT

Information on patent family members

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| EP 0905518 | A 31-03-1999 | NONE | |